

REMARKS

I. Amendments

By this amendment, claims 12, 18, 23 and 28 have been amended.

This amendment adds no new matter to the specification. Support for this amendment is found in the specification and claims as filed.

In particular, support for the modifications of claims 18 and 23 may be found in the specification at page 18, line 34- page 19, line 30 *inter alia*.

No amendment of inventorship is necessitated by this amendment.

II. Discussion of the Rejection of Claim 12 under 35 U.S.C. Sec. 112, First Paragraph

Claim 12 has been rejected under 35 U.S.C. Sec. 112, first paragraph for allegedly failing to comply with the enablement requirement. Specifically, the Examiner does not believe that the specification supports the recited prevention of certain conditions. Applicants respectfully traverse the rejection.

To advance prosecution, claim 12 has been amended to delete “preventing or” thus rendering the present rejection moot.

Therefore Applicants respectfully request withdrawal of the Sec. 112, first paragraph rejection.

III. Discussion of the Rejection of Claim 18 under 35 U.S.C. Sec. 112, First Paragraph

Claim 18 has been rejected under 35 U.S.C. Sec. 112, first paragraph because the specification, while allegedly being enabling for pioglitazone; compounds of the formula II, does not reasonably provide enablement for other insulin sensitizers, such as metformin. Applicants respectfully traverse the rejection.

By this amendment, claim 18 has been amended to recite specific insulin sensitizers.

Therefore Applicants respectfully request withdrawal of the Sec. 112, first paragraph rejection.

IV. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) Kemnitz *et al.*, Momose *et al.*, and Acton III *et al.*

Claims 9-12, 18 and 28-30 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly being unpatentable over Kemnitz *et al.* (Diabetes 1994 article), Momose *et al.* (U.S. Patent 6,251,926) and Acton III *et al.* (2002/0042441). Applicants respectfully traverse the rejection.

Applicants believe that by virtue of the priority date of their Japanese patent application, which is April 14, 1999; that neither Momose *et al.* or Acton III *et al.* are proper art.

As concerns Kemnitz *et al.*, it teaches that pioglitazone hydrochloride is useful as an antidiabetic. However, just because a compound is useful as an anti-diabetic agent, there is no automatic assumption that the same compound is useful to treat acidosis. In fact, some antidiabetic compounds actually *cause* acidosis, as indicated on page 26, lines 1 and 2 of the specification.

As stated above, it is well established that anti-diabetic agents are not always useful to treat acidosis. This is particularly true in the case of biguanides. The Examiner is requested to consider that 1) in the cited reference of Acton III *et al.*, it is stated that "The biguanides increase insulin sensitivity resulting in some correction of hyperglycemia. However, the two biguanides, phenformin and metformin, can induce lactic acidosis and nausea/diarrhea, respectively" on page 1, right-hand column, lines 7-10; and 2) the additionally cited reference of Sirtori *et al.* teaches that "Metformin, similarly to the other biguanide phenformin, has been related as potentially dangerous, because of the possible induction of lactic acidosis, in some cases with a fatal outcome." on page 187, lines 10-13 in the Summary, in support of Applicants' argument.

For this reason, Applicants assert that the method set forth in independent claim 18 as amended is neither taught nor suggested by Kemnitz *et al.*

Claims 9-12 and 28-30 depend upon claim 18. Applicants submit that the more specific dependent claims are also not rendered obvious by the teachings of the cited reference for the reason provided above.

Therefore, Applicants respectfully request withdrawal of the Sec. 103(a) rejection of claims 9-12, 18 and 28-30.

V. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) Kemnitz *et al.*, Inoue *et al.*, or Fujiwara *et al.*

Claims 16 and 23-27 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly being unpatentable over Kemnitz *et al.* (Diabetes 1994 article), Inoue *et al.* (Metabolism Clinical and Experimental 1995 article) or Fujiwara *et al.* (Diabetes 1988 article) in view of Windholz *et al* (The Merck Index). Applicants respectfully traverse the rejection.

In Kemnitz *et al.*, it is taught that pioglitazone hydrochloride is useful as an antidiabetic agent; in Inoue *et al.*, it is taught that troglitazone effects insulin sensitivity; and in Fujiwara *et al* it is taught that a thiazolidinedione is an antidiabetic agent. Each reference teaches an insulin sensitizer for treatment of diabetes, as the Examiner has indicated.

However, just because a compound is useful as an anti-diabetic agent, there is no automatic assumption that the same compound is useful to treat acidosis. In fact, some antidiabetic compounds actually *cause* acidosis, as indicated on page 26, lines 1 and 2 of the specification. Applicants hereby incorporate their arguments from Sec. IV above with respect to this point.

Not only do none of the references teach or suggest compounds for the treatment of acidosis, but also none of the three cited references teaches or suggests the presently claimed *combination* for improving or treating acidosis. Applicants assert that the method set forth in independent claim 16 as amended is neither taught nor suggested by Kemnitz *et al*, Inoue *et al* or Fujiwara *et al.*

The deficiencies of Kemnitz *et al*, Inoue *et al* or Fujiwara *et al.* are not remedied by the teachings of The Merck Index, in giving a definition of insulin. The Merck Index merely lists insulin as an antidiabetic. Not only is the reference silent on treating acidosis, but also there is not even an indication that insulin can treat complications of diabetes in the cited reference. Therefore, the combined teachings of The Merck Index with Kemnitz *et al*, Inoue *et al* or Fujiwara *et al* does not teach or suggest the aspects of the invention set forth in independent claim 16.

Claims 23-27 depend upon claim 16. Applicants submit that the more specific dependent claims are also not rendered obvious by the combined teachings of the cited reference for the reason provided above.

Therefore, Applicants respectfully request withdrawal of the Sec. 103(a) rejection of claims 16 and 23-27.

VI. Discussion of the Additionally Cited Reference

Applicants wish to thank the Examiner for bringing the additionally cited reference of Sirtori *et al.* to their attention. Applicants have carefully reviewed this reference and do not believe that it detracts from the patentability of the subject invention.

VII. Conclusion

Reconsideration and allowance of the claims as amended is requested. Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, he is respectfully requested to call Applicants' attorney at (847) 383-3391.

Respectfully submitted,

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